```
=> herpesvirus (s) DNA vaccine
          25030 HERPESVIRUS
           1908 HERPESVIRUSES
          25466 HERPESVIRUS
                  (HERPESVIRUS OR HERPESVIRUSES)
         796739 DNA
          18832 DNAS
         799684 DNA
                  (DNA OR DNAS)
          58265 VACCINE
          59079 VACCINES
          72842 VACCINE
                  (VACCINE OR VACCINES)
           4566 DNA VACCINE
                  (DNA(W)VACCINE)
L8          125 HERPESVIRUS (S) DNA VACCINE

=> gold (s) particle
         234090 GOLD
             84 GOLDS
         234107 GOLD
                  (GOLD OR GOLDS)
         715439 PARTICLE
         792866 PARTICLES
        1198655 PARTICLE
                  (PARTICLE OR PARTICLES)
L9        10817 GOLD (S) PARTICLE

=> L9 and l8
L10           5 L9 AND L8

=> genomic and L8
         107964 GENOMIC
          13474 GENOMICS
         117643 GENOMIC
                  (GENOMIC OR GENOMICS)
L11           1 GENOMIC AND L8

=> artificial chromoson
         154890 ARTIFICIAL
              4 ARTIFICIALS
         154893 ARTIFICIAL
                  (ARTIFICIAL OR ARTIFICIALS)
              1 CHROMOSON
L12           0 ARTIFICIAL CHROMOSON
                  (ARTIFICIAL(W)CHROMOSON)

=> (artificial bacterial chromoson)
         154890 ARTIFICIAL
              4 ARTIFICIALS
         154893 ARTIFICIAL
                  (ARTIFICIAL OR ARTIFICIALS)
         261719 BACTERIAL
             47 BACTERIALS
         261750 BACTERIAL
                  (BACTERIAL OR BACTERIALS)
              1 CHROMOSON
L13           0 (ARTIFICIAL BACTERIAL CHROMOSON)
                  (ARTIFICIAL(W)BACTERIAL(W)CHROMOSON)

=> ABC
          11579 ABC
            122 ABCS
L14       11656 ABC
```

(ABC OR ABCS)

=> vector and L14
161625 VECTOR
102438 VECTORS
220492 VECTOR
(VECTOR OR VECTORS)
L15 320 VECTOR AND L14

=> L8 and L15
L16 0 L8 AND L15

=> D L11 IBIB ABS 1

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:338390 CAPLUS
DOCUMENT NUMBER: 134:352268
TITLE: DNA-vaccines based on constructs derived from the genomes of human and animal pathogens
INVENTOR(S): Swain, William F.; Roberts, Lee K.; Payne, Lendon G.; Braun, Ralph P.
PATENT ASSIGNEE(S): Powderject Vaccines, Inc., USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001032221 | A1 | 20010510 | WO 2000-US30282 | 20001102 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2389693 | AA | 20010510 | CA 2000-2389693 | 20001102 |
| EP 1225920 | A1 | 20020731 | EP 2000-975552 | 20001102 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2003528816 | T2 | 20030930 | JP 2001-534425 | 20001102 |
| AU 785066 | B2 | 20060914 | AU 2001-13591 | 20001102 |
| PRIORITY APPLN. INFO.: | | | US 1999-432361 A | 19991103 |
| | | | WO 2000-US30282 W | 20001102 |

AB Methods of eliciting an immune response in a subject by administering one or more large genomic DNA fragments are provided. Also provided are methods of identifying sequences encoding antigenic polypeptides. Also provided are vaccine compns. comprising one or more large genomic DNA fragments.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L10 IBIB ABS 105
5 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):1-5

L10 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1261796 CAPLUS

DOCUMENT NUMBER: 144:21828
TITLE: Adjuvant compositions and particle-delivered codon-optimized DNA vaccines encoding HIV antigens, useful in prophylaxis and treatment of HIV infections
INVENTOR(S): Braun, Ralph Patrick; Thomsen, Lindy; Van-Wely, Catherine; Ertl, Peter
PATENT ASSIGNEE(S): Powdermed Limited, UK; Glaxo Group Limited
SOURCE: U.S. Pat. Appl. Publ., 75 pp., Cont.-in-part of U.S. Ser. No. 102,622.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2005266024 | A1 | 20051201 | US 2005-507928 | 20050509 |
| US 2003190308 | A1 | 20031009 | US 2002-102622 | 20020319 |
| WO 2003080112 | A2 | 20031002 | WO 2003-GB1213 | 20030319 |
| WO 2003080112 | A3 | 20031106 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005256070 | A1 | 20051117 | US 2005-29465 | 20050106 |
| PRIORITY APPLN. INFO.: | | | US 2002-102622 A2 | 20020319 |
| | | | US 2002-366058P P | 20020319 |
| | | | WO 2003-GB1213 W | 20030319 |

OTHER SOURCE(S): MARPAT 144:21828
AB The present invention relates to certain adjuvant compns., and to vaccine and/or nucleic acid immunization strategies employing such compns. The invention in particular relates to DNA vaccines that are useful in the prophylaxis and treatment of HIV infections, more particularly when administered by particle mediated delivery. The examples disclose the use of imiquimod, in the form of Aldara cream, to enhance immune response to DNA vaccines encoding viral antigens, epitopes and fusions thereof. Also disclosed is the optimization of the viral coding sequences to more closely resemble the codon usage of highly expressed human genes. Methods used include gold particle-mediated immunization of plasmid DNA using "gene gun" DNA cartridges.

L10 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:451540 CAPLUS
DOCUMENT NUMBER: 143:6270
TITLE: DNA vaccines with enhanced potency employing nucleic acid encoding IPP (immunogenicity-potentiating peptides) and anti-apoptotic proteins
INVENTOR(S): Wu, Tzyy-Choou; Hung, Chien Fu; Kim, Tae-Woo
PATENT ASSIGNEE(S): Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| WO 2005047501 | A1 | 20050526 | WO 2004-US5292 | | 20040224 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-449429P P 20030224
US 2003-488527P P 20030718
US 2003-533792P P 20031231

AB As the present inventors discovered, in addition to DNA encoding an antigen, the concomitant administration of a second DNA mol. encoding an anti-apoptotic protein enhances the magnitude and/or duration of a T cell mediated immune response, and potentiates a desired clin. effect - such as eradication of an existing tumor or prevention of the spread or metastasis of a tumor. In prefered embodiment, T cell immune responses are also enhanced by presentation of antigen to CD8+ T cells using a chimeric nucleic acid immunogen or vaccine that links DNA encoding an antigen with DNA encoding a polypeptide that targets or translocates the antigenic polypeptide to which it is fused (immunogenicity-potentiating polypeptides or 'IPP'). By inhibiting apoptosis in the vicinity of a T cell responses to such a nucleic acid immunogen, even more potent immune responses are attained. The present strategy prolongs the survival of DNA-transduced cells, including dendritic cells (DCs), thereby enhancing the priming of antigen-specific T cells and increase potency. Co-delivery of DNA encoding an inhibitor of apoptosis, including (a) BCL-xL, (b) BCL-2, (c) XIAP, (d) dominant neg. caspase-9, or (e) dominant neg. caspase-8, or (f) serine protease inhibitor 6 (SPI-6) which inhibits granzyme B, with DNA encoding an antigen, prolongs the survival of transduced DCs and results in significant enhancement of antigen-specific T cell immune responses that provide potent antitumor effects. Thus, co-administration of a DNA vaccine encoding antigen linked to an IPP along with one or more DNA constructs encoding an anti-apoptotic protein provides a novel way to enhance vaccine potency.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:756383 CAPLUS

DOCUMENT NUMBER: 137:246257

TITLE: A DNA vaccine containing an infectious Marek's disease virus genome can confer protection against tumorigenic Marek's disease in chickens

AUTHOR(S): Tischer, B. Karsten; Schumacher, Daniel; Beer, Martin; Beyer, Jorg; Teifke, Jens Peter; Osterrieder, Kerstin; Wink, Kerstin; Zelnik, Vladimir; Fehler, Frank; Osterrieder, Nikolaus

CORPORATE SOURCE: Institute of Molecular Biology, Federal Research Centre for Virus Diseases of Animals, Friedrich-Loeffler-Institutes, Insel Riems, D-17498, Germany

SOURCE: Journal of General Virology (2002), 83(10), 2367-2376
CODEN: JGVIAY; ISSN: 0022-1317

PUBLISHER: Society for General Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A DNA vaccine containing the infectious BAC20 clone of serotype 1 Marek's disease virus (MDV) was tested for its potential to protect against Marek's disease (MD). Chickens were immunized at 1 day old with BAC20 DNA

suspended either in PBS, as calcium phosphate ppts., incorporated into chitosan nanoparticles, in Escherichia coli DH10B cells, or bound to gold particles for gene-gun delivery. Challenge infection with MDV strain EU1 was performed at 12 days old, and four out of seven birds immunized with BAC20 DNA in saline by the i.m. route remained free of MD until day 77 after challenge infection. A delay in the development of the disease could be observed in some animals vaccinated with other BAC20 DNA formulations, but clin. MD and tumor formation were evident in all but one bird. Five out of seven animals immunized with the vaccine virus CVI988 were protected against MD, but none out of seven birds survived EU1 challenge infection after injection of neg.-control plasmid DNA. In a second animal experiment, five out of 12 chickens immunized with BAC20 DNA and six out of eight birds immunized with virus reconstituted from BAC20 DNA remained free of MD after challenge infection. In contrast, none out of 12 chickens survived challenge infection after immunization with BAC20 DNA lacking the essential gE gene or with gE-neg. BAC20 virus. The results suggested that an MDV BAC DNA vaccine has potential to protect chickens against MD, but that in vivo reconstitution of vaccine virus is a prerequisite for protection.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:300884 CAPLUS
DOCUMENT NUMBER: 134:339526
TITLE: Sequences of chimeric DNA vaccine with enhanced anticancer potency
INVENTOR(S): Wu, Tzyy-choou; Hung, Chien-fu
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001029233 | A2 | 20010426 | WO 2000-US41422 | 20001020 |
| WO 2001029233 | A3 | 20020207 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6734173 | B1 | 20040511 | US 2000-501097 | 20000209 |
| CA 2388045 | AA | 20010426 | CA 2000-2388045 | 20001020 |
| EP 1222289 | A2 | 20020717 | EP 2000-986821 | 20001020 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2004500047 | T2 | 20040108 | JP 2001-532216 | 20001020 |
| AU 784605 | B2 | 20060511 | AU 2001-22994 | 20001020 |
| US 2004086845 | A1 | 20040506 | US 2002-115440 | 20020404 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1999-421608 | A2 | 19991020 |
| US 2000-501097 | A2 | 20000209 |
| WO 2000-US41422 | W | 20001020 |
| US 2001-281003P | P | 20010404 |

AB The invention provides novel chimeric nucleic acids encoding a chimeric polypeptide, constructs for expressing these polypeptides both in vitro and in vivo, isolated chimeric polypeptides, pharmaceutical compns. and

methods of making and using these compns. These compns. and methods are particularly useful for stimulating or enhancing the immunogenicity of a selected antigen or stimulating or enhancing a cellular immune response specific for that antigen. The nucleic acid of the invention comprises a first polypeptide domain comprising a carboxy terminal fragment of a heat shock protein (HSP), an Flt-3 ligand (FL), a cytoplasmic translocation domain of a Pseudomonas exotoxin A (ETA dII), or a granulocyte-macrophage-colony stimulating factor (GM-CSF) sequence, and a second polypeptide domain comprising an antigenic polypeptide.

L10 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:800031 CAPLUS
DOCUMENT NUMBER: 132:106631
TITLE: Particle-mediated DNA immunization of cattle confers long-lasting immunity against bovine herpesvirus-1
AUTHOR(S): Braun, R. P.; Babiuk, L. A.; Loehr, B. I.; van Drunen Littel-van den Hurk, S.
CORPORATE SOURCE: Veterinary Infectious Disease Organization, University of Saskatchewan, Saskatoon, SK, S7N 5E3, Can.
SOURCE: Virology (1999), 265(1), 46-56
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Particle-mediated delivery was used as a method to vaccinate ruminants with a DNA vaccine. The optimal conditions for gene gun-based delivery of gold particles into the epidermal layer of the skin were determined After delivery of the gold particles, an inflammatory response was observed This response occurred regardless of the presence of plasmid and therefore was a result of the phys. disturbance of the skin by the gold particles. To identify transfected cells, a plasmid expressing a green fluorescent protein was delivered into the skin. Fluorescent cells were located primarily in the outermost layers of the epidermis and outside the core of gold particles deposited by the gene gun. Cattle were immunized by gene gun with a plasmid expressing a truncated, secreted form of bovine herpesvirus-1 glycoprotein D. Serum antibody responses, antigen-specific proliferation, and interferon-γ secretion by peripheral blood lymphocytes were demonstrated. These immune responses were of long duration and sufficient magnitude to protect cattle against challenge with bovine herpesvirus-1, which demonstrates the efficacy of gene gun-based delivery of DNA vaccines to target species.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE
COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 82.77 | 82.98 |

=> HSV (s) DNA vaccine
L14 83 HSV (S) DNA VACCINE

=> gold (s) particle
L15 14082 GOLD (S) PARTICLE

=> L15 and L14
L16 2 L15 AND L14

=> D L16 IBIB Abs 1-2

L16 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:728926 CAPLUS
DOCUMENT NUMBER: 132:48709
TITLE: BAC-VAC, a novel generation of (DNA) vaccines: A bacterial artificial chromosome (BAC) containing a replication-competent, packaging-defective virus genome induces protective immunity against herpes simplex virus 1
AUTHOR(S): Suter, Mark; Lew, Andrew M.; Grob, Philipp; Adema, Gosse J.; Ackermann, Mathias; Shortman, Ken; Fraefel, Cornel
CORPORATE SOURCE: Institute of Virology, University of Zurich, Zurich, CH-8057, Switz.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(22), 12697-12702
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study aimed to exploit bacterial artificial chromosomes (BAC) as large antigen-capacity DNA vaccines (BAC-VAC) against complex pathogens, such as herpes simplex virus 1 (HSV-1). The 152-kbp HSV-1 genome recently has been cloned as an F-plasmid-based BAC in Escherichia coli (fHSV), which can efficiently produce infectious virus progeny upon transfection into mammalian cells. A safe modification of fHSV, fHSVΔpac, does not give rise to progeny virus because the signals necessary to package DNA into virions have been excluded. However, in mammalian cells fHSVΔpac DNA can still replicate, express the HSV-1 genes, cause cytotoxic effects, and produce virus-like particles. Because these functions mimic the lytic cycle of the HSV-1 infection, fHSVΔpac was expected to stimulate the immune system as efficiently as a modified live virus vaccine. To test this hypothesis, mice were immunized with fHSVΔpac DNA applied intradermally by gold-particle bombardment, and the immune responses were compared with those induced by infection with disabled infectious single cycle HSV-1. Immunization with either fHSVΔpac or disabled infectious single cycle HSV-1 induced the priming of HSV-1-specific cytotoxic T cells and the production of virus-specific antibodies and conferred protection against intracerebral injection of wild-type HSV-1 at a dose of 200 LD50. Protection probably was cell-mediated, as transfer of serum from immunized mice did not protect naive animals. We conclude that BAC-VACs per se, or in combination with genetic elements that support replicative amplification of the DNA in the cell nucleus, represent a useful new generation of DNA-based vaccination strategies for many viral and nonviral antigens.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:31163 BIOSIS
DOCUMENT NUMBER: PREV200000031163
TITLE: BAC-VAC, a novel generation of (DNA) vaccines: A bacterial artificial chromosome (BAC) containing a

replication-competent, packaging-defective virus genome induces protective immunity against herpes simplex virus 1.

AUTHOR(S): Suter, Mark [Reprint author]; Lew, Andrew M.; Grob, Philipp; Adema, Gosse J.; Ackermann, Mathias; Shortman, Ken; Fraefel, Cornel

CORPORATE SOURCE: Institute of Virology, University of Zurich, Winterthurerstrasse 266a, CH-8057, Zurich, Switzerland

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (Oct. 26, 1999) Vol. 96, No. 22, pp. 12697-12702. print.
CODEN: PNASA6. ISSN: 0027-8424.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 13 Jan 2000
Last Updated on STN: 31 Dec 2001

AB This study aimed to exploit bacterial artificial chromosomes (BAC) as large antigen-capacity DNA vaccines (BAC-VAC) against complex pathogens, such as herpes simplex virus 1 (HSV-1). The 152-kbp HSV-1 genome recently has been cloned as an F-plasmid-based BAC in Escherichia coli (fHSV), which can efficiently produce infectious virus progeny upon transfection into mammalian cells. A safe modification of fHSV, fHSVDELTApac, does not give rise to progeny virus because the signals necessary to package DNA into virions have been excluded. However, in mammalian cells fHSVDELTApac DNA can still replicate, express the HSV-1 genes, cause cytotoxic effects, and produce virus-like particles. Because these functions mimic the lytic cycle of the HSV-1 infection, fHSVDELTApac was expected to stimulate the immune system as efficiently as a modified live virus vaccine. To test this hypothesis, mice were immunized with fHSVDELTApac DNA applied intradermally by gold-particle bombardment, and the immune responses were compared with those induced by infection with disabled infectious single cycle HSV-1. Immunization with either fHSVDELTApac or disabled infectious single cycle HSV-1 induced the priming of HSV-1-specific cytotoxic T cells and the production of virus-specific antibodies and conferred protection against intracerebral injection of wild-type HSV-1 at a dose of 200 LD50. Protection probably was cell-mediated, as transfer of serum from immunized mice did not protect naive animals. We conclude that BAC-VACs per se, or in combination with genetic elements that support replicative amplification of the DNA in the cell nucleus, represent a useful new generation of DNA-based vaccination strategies for many viral and nonviral antigens.